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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/914,621 | 12/26/2001 | Xiaomao Li | 1038-1191MIS:JB | 8175 |

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| EXAMINER | |
|---|---|
| NGUYEN, QUANG | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/914,621 | LI ET AL. | |
| | Examiner | Art Unit | |
| | Quang Nguyen, Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicants' amendment filed on 9/17/03 has been entered.

Amended claims 1-11 are pending in the present application, and they are examined on the merits herein.

### *Claim Objections*

Amended claim 1 is objected to because of the term "a respiratory syncytial virus" does not represent (RSV F). What does the F stand for? Correction is required.

Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is noted that claim 1 is already directed to a plasmid vector.

### *Oath/Declaration*

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration (see change in the Post Office Address of Mary E. Ewasyshyn). See 37 CFR 1.52(c).

***Specification***

The disclosure is objected to because on page 10, line 9, there is no Brief Description for Figure 11 in the specification. However, there are Figures 11A-I in the specification.

Appropriate correction is required in the Brief description of the Figures.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new ground of rejection necessitated by Applicants' amendment.**

Claim 3 recites the limitation "said first nucleotide sequence encodes a RSV F protein fragment" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim. It is noted in the base claim 1 which claim 3 is dependent on, there is no recitation of any first nucleotide sequence, nor is there any sequence encoding a RSV F protein fragment. Clarification is requested because the metes and bounds of the claim are not clearly determined.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Amended claims 1, 3-9 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Li et al. (J. Exp. Med. 188:681-688, 1998; IDS) for the same reasons already set forth in the previous Office Action mailed on 3/17/03 (pages 9-10).

Li et al. teach the preparation of optimized plasmid DNA vectors expressing the Respiratory syncytial virus (RSV) fusion F protein (DNA-F), and demonstrate that they are as effective as live RSV in mice at inducing neutralizing antibody and cytotoxic T lymphocyte responses, protection against infection (see abstract). The plasmid vector constructs (pXL1-pXL4) include expression of full length and truncated RVS F (without a transmembrane coding region) proteins under the control of CMV promoter in the presence or absence of the rabbit β-globin intron II sequence upstream of the F-protein encoding sequence (see Construction of plasmids expressing the RSV F proteins on page 682, col. 1; and page 683). For intramuscular immununization, each of the plasmid vectors was injected into mice 2 X 50 μg (1 μg/μl in phosphate buffered solution or PBS which is a pharmaceutically acceptable carrier), and for intradermal immunization 100 μg of pXL2 was injected near the base of the tail (page 682, col. 2, first paragraph). Li et al. teach specifically that further modification of the above vectors can be made by using a more effective signal peptide (which is not an autologous signal

peptide of F protein) for enhanced F protein expression/secretion so that the pre-treatment step of muscle tissue with cardiotoxin (to increase DNA uptake and enhance immune response) before immunization with DNA F-vectors can be eliminated (page 684, col. 2, first paragraph).

Accordingly, the teachings of Li et al. meet every limitation of the instant claims. Therefore, Li et al. anticipate the instant claimed invention.

***Response to Arguments***

Applicants' argument related to the above rejection in the Amendment filed on 9/17/03 (page 6) has been fully considered, but it is not found persuasive.

Applicants argue that Li et al. is not a prior art under 35 USC 102(a) as evidenced by a Declaration under 37 CFR 1.131, indicating that the invention which is the subject matter of this application was made prior to the effective date of the reference and that the non-inventor authors of the Li et al. are not the inventors of the subject matter hereof.

It is noted that the Declaration is unsigned. If the Declaration was signed, it would be sufficient to overcome the above rejection. Therefore, claims 1, 3-9 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Li et al. for the reasons set forth above.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (J. Exp. Med. 188:681-688, 1998; IDS) in view of Li et al. (WO 99/04010; IDS) and Lee et al. (Molecules and Cells 8:444-451, 1998; IDS) for the same reasons already set forth in the previous Office Action mailed on 3/17/03 (pages 10-14).

Li et al. (J. Exp. Med.) teach the preparation of optimized plasmid DNA vectors expressing the Respiratory syncytial virus (RSV) fusion F protein (DNA-F), and demonstrate that they are as effective as live RSV in mice at inducing neutralizing antibody and cytotoxic T lymphocyte responses, protection against infection (see abstract). The plasmid vector constructs (pXL1-pXL4) include expression of full length and truncated RVS F (without a transmembrane coding region) proteins under the

control of CMV promoter in the presence or absence of the rabbit β-globin intron II sequence upstream of the F-protein encoding sequence (see Construction of plasmids expressing the RSV F proteins on page 682, col. 1; and page 683). For intramuscular immununization, each of the plasmid vectors was injected into mice 2 X 50 μg (1 μg/μl in phosphate buffered solution or PBS which is a pharmaceutically acceptable carrier), and for intradermal immunization 100 μg of pXL2 was injected near the base of the tail (page 682, col. 2, first paragraph). Li et al. teach specifically that further modification of the above vectors can be made by using a more effective signal peptide (which is not an autologous signal peptide of F protein) for enhanced F protein expression/secretion so that the pre-treatment step of muscle tissue with cardiotoxin (to increase DNA uptake and enhance immune response) before immunization with DNA F-vectors can be eliminated (page 684, col. 2, first paragraph).

Li et al. (J. Exp. Med.) do not explicitly teach the use of HSV-1 gD signal sequence as the effective signal peptide, or substituting a nucleotide sequence encoding the autologous RSV F signal peptide sequence with a nucleotide sequence encoding a heterologous signal peptide, preferably HSV-1 gD signal peptide, for the modified plasmid vectors.

However, at the effective filing date of the present application, Li et al. (WO 99/04010) already teach the preparation of a plasmid vector encoding a G protein of RSV, wherein a heterologous viral or eukaryotic signal peptide such as human tissue plasminogen activator signal peptide replaces the endogenous signal peptide of the

RSV G protein (line 31 of page 15) and the use of such a vector to immunize a host against RSV infection.

Additionally, Lee et al. teach the replacement of each of the signal sequences of hepatitis C virus (HCV) envelope proteins with the signal sequence of herpes simplex virus type-1 (HSV-1) gD for an efficient expression and secretion of HCV envelope proteins in an HCV envelope plasmid vector-based immunization approach (see abstract, and Fig. 1). Lee et al. further note that the N-terminal fusion of a signal sequence from gD into HIV-1 gp160 has been shown to be expressed and secreted efficiently (page 446, col. 1, last 3 lines).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the plasmid vectors and methods taught by Li et al. (J. Exp. Med.) by substituting a nucleotide sequence encoding the autologous RSV F signal peptide sequence with a nucleotide sequence encoding a heterologous signal peptide, including the HSV-1 gD signal peptide for enhancing the F protein expression/secretion in a host in light of the teachings of Li et al. (WO 99/04010) and Lee et al. This is because Li et al. (J. Exp. Med.) specifically teach to use a more effective signal peptide for enhanced F protein expression/secretion in a host so that the pre-treatment step with cardiotoxin could be avoided, and that the use of HSV-1 gD signal peptide for an efficient expression and secretion of HIV-1 gp160 and HCV envelope proteins has been demonstrated in the art as taught by Li et al. (WO 99/04010), coupled with the teachings of Li et al. (WO 99/04010) to use a heterologous viral or eukaryotic signal peptide such as human tissue plasminogen activator signal peptide for replacing the endogenous signal peptide of the

RSV G protein (line 31 of page 15) in the preparation of a plasmid vector and the use of such a vector to immunize a host against RSV infection. The modified plasmid vectors containing HSV-1 gD signal encoded sequence in place of the sequence coding for the autologous RSV F signal peptide would have the same features as the plasmid vector p82M35B.

One of ordinary skilled artisan would have been motivated to carry out the above modification because Li et al. (J. Exp. Med.) specifically teach to use a more effective signal peptide for enhanced F protein expression/secretion in a host so that the pre-treatment step with cardiotoxin could be avoided, and that the use of HSV-1 gD signal peptide for an efficient expression and secretion of HIV-1 gp160 and HCV envelope proteins has been demonstrated in the art as taught by Li et al. (WO 99/04010).

One of ordinary skilled artisan would have a reasonable expectation of success because the use of HSV-1 gD signal peptide for an efficient expression and secretion of HIV-1 gp160 and HCV envelope proteins has already been demonstrated in the art as taught by Li et al. (WO 99/04010)

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

***Response to Arguments***

Applicants' argument related to the above rejection in the Amendment filed on 9/17/03 (pages 6-7) has been fully considered, but it is not found persuasive.

Applicants argue that Li et al. is not a prior art as evidenced by a Declaration under 37 CFR 1.131, indicating that the invention which is the subject matter of this application was made prior to the effective date of the reference and that the non-inventor authors of the Li et al. are not the inventors of the subject matter hereof.

It is noted that the Declaration is unsigned. Therefore, claims 1-2 remain rejected for the reasons set forth above.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended claims 1-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,083,925. Although the conflicting claims are not identical, they are not

patentably distinct from each other for the reasons already set forth in the previous Office Action (pages 15-16).

***Response to Arguments***

Applicants' argument related to the above rejection in the Amendment filed on 9/17/03 (page 7) has been fully considered, but it is not found persuasive.

Applicants argue that the pending claims are drawn to a plasmid vector and to an immunogenic composition which are not found in U.S. Patent No. 6,083,925, and therefore the claimed subject matter is not an obviousness-type double patenting of U.S. Patent No. 6,083,925.

It is noted that a method of immunizing and a method of using a gene in U.S. Patent No. 6,083,925 utilize the same plasmid vector and immunogenic composition of the presently claimed invention. Furthermore, the plasmid vector and the immunogenic composition of the present invention can only be used in the methods of issued U.S. Patent No. 6,083,925. Therefore, in order for an ordinary skilled artisan to practice the methods in the aforementioned issued U.S. Patent, the artisan must also possess the same plasmid vector and the same immunogenic composition. Additionally, Examiner notes that there was no restriction requirement issued during the prosecution of the U.S. Patent No. 6,083,925.

Claims 1-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No.

6,486,135. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons already set forth in the previous Office Action (pages 16-17).

***Response to Arguments***

Applicants' argument related to the above rejection in the Amendment filed on 9/17/03 (pages 7-8) has been fully considered, but it is not found persuasive.

Applicants argue that the pending claims are drawn to a plasmid vector and to an immunogenic composition which are not found in U.S. Patent No. 6,486,135, and therefore the claimed subject matter is not an obviousness-type double patenting of U.S. Patent No. 6,486,135.

It is noted that a method of using a gene in U.S. Patent No. 6,486,135 utilize the same plasmid vector and immunogenic composition of the presently claimed invention. Furthermore, the plasmid vector and the immunogenic composition of the present invention can only be used in the method of issued U.S. Patent No. 6,486,135. Therefore, in order for an ordinary skilled artisan to practice the method in the aforementioned issued U.S. Patent, the artisan must also possess the same plasmid vector and the same immunogenic composition. Additionally, Examiner notes that a terminal disclaimer for U.S. Patent NO. 6,083,925 has also been filed during the prosecution of U.S. Patent No. 6,486,135.

## *Conclusions*

***No claims are allowed.***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

*Quang Nguyen, Ph.D.*

DAVID GUZO
PRIMARY EXAMINER